THE INTERVIEW

Drs. Leguyader and Epps are thanked by the applicant for a most cordial and helpful interview granted to his attorney on March 11, 2002, and Dr. Epps' for the subsequent telephonic conferences held to discuss three patents she provided that are relevant to this case. US Patent Nos. 5,733,572 to Unger et al.; 5,756,353 to Debs et al.; 5,049,388 to Knight et al.;and 5,616,334 to Janoff et al., resulting from an up-dated search, were cited by the examiner. These references are individually discussed below. Suffice it to say, however, that neither reference by itself, nor their combination, render the claimed invention obvious. The present claim language was discussed during the interview and subsequent conferences with Dr. Epps, and it was agreed that, pending a final review of the applicant's remarks, it would suffice to overcome the outstanding rejections. The following remarks contain a summary, and an expansion, of the arguments made by the applicant to the examiner(s).

THE CLAIM AMENDMENTS

The claims have been amended to place them in proper form for allowance. The claim amendments are fully supported by the specification as filed, and by the original claims.

Claim 108 has been amended to make the presence of a surfactant optional when the target is the adenosine A2a or A2b receptors. These targets were not covered by the claims ineither of the parent applications and, therefore, the applicant wishes to include in the composition just the nucleic acid, and optionally the surfactant. Claims 146, 148 and 152 have been amended to indicate that the aerosol or spray is formed upon delivery. The independent claims directed to a device, a kit and a method of delivering have been amended to encompass a non-liposomal composition broadly comprising nucleic acid. The use of liposomes in the composition is supported, for example, at page 45, lines 22-23, of the specification, and the original claims. A range of particle size "about 0.5 to 500 μ" is supported by the description of these two points of the range in the specification enabling the creation of a broad range of particle sizes in light of Ex parte Jackson, 110 USPQ 561 (1956); Ex parte Batchelder and Zimmermann, 181 USPQ 38 (1960); Ex parte Lawrence, 131 USPQ 40 (1960); In re Welstead, 174 USPQ 449 (1972). Copies enclosed.

The addition of the oligo having an effect on "levels of adenosine receptors" is supported throughout the specification, and more particularly by the composition claims describing that the oligos are targeted to such receptors. The description of the surfactant, for example in claim 190, is supported by the description and the original claims, which list a series of different surfactants,

from which the broad groups where named. See, deleted language of the same claim. The added sequence numbers in claim 231 correspond to sequences of the adenosine A2a and A2b receptor targets, and are supported at page 38-40 of the original application. The remaining amendments have been undertaken to clean up the text of the claims as previously agreed to.

The amendments to the claims are fully supported by the specification as filed and the original claims. No new matter is believed to be present in the pending claims. The applicant, thus, believes they are in condition for allowance.

THE NEWLY CITED REFERENCES

The examiner updated the search in this application, and provided the applicant with the following references: US Patent No. 5,616,334 to Janoff et al., US Patent No. 5,756,353 to Debs, US Patent No. 5,049,388 to Knight et al., and US Patent No. 5,733,572 to Unger et al. these references were cited in a rejection of claim 173 et seq. under 35 USC 1.103. These grounds of rejection are traversed by the applicant.

Of the references uncovered by the examiner recently, the Knight patent provides a particle size range as applied to protein molecules, not nucleic acids, and the Unger et al., Janoff, and Debs patents describe and claim liposome-nucleic acid complexes (Debs), gas filled, lipid microspheres (Unger et al.), and liposomes (but not lipid-drug complexes) associated with "nucleic acids such as thymine (sic) and polynucleotides such as RNA" (Janoff et al.) (See, col. 9, ls. 62-63). Although Janoff et al. also describe lipid-drug complexes, they require that the drug in these complexes be hydrophobic. See, col.9, ls. 33-35. The present agent is hydrophilic and, therefore, it may be said that Janoff et al. teach away from the claimed invention, where a non-liposomal surfactant may be added to the composition for delivery as directed by claim 173, or by the independent claims directed to a device or a kit.

The applicant, thus submits that the claimed invention is patentably distinguishable over each of these patents, and over their combination.

GENERAL REMARKS

The Assistant Commissioner is hereby authorized to charge $200.- for a two-month extension of time, and any other fees owed, or refund any excess, to PTO Deposit Account No. 50-

1728.

In view of the foregoing amendments and remarks, as well as a Petition for Extension of Time and a Notice of Appeal with payment of the requisite fee, this application is believed to be in condition for allowance. Early notice to this respect is solicited.

Respectfully submitted.
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June 12, 2002
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or suspensions of the active ingredient into a therapeutic aerosol mist either by means of acceleration of a compressed gas, typically air or oxygen, through a narrow venturi orifice or by means of ultrasonic agitation. Suitable formulations for use in nebulizers comprise the active ingredient in a liquid carrier in an amount of up to 40% w/w preferably less than 20% w/w of the formulation. The carrier is typically water or a dilute aqueous alcoholic solution, preferably made isotonic with body fluids by the addition of, for example, sodium chloride. Optional additives include preservatives if the formulation is not prepared sterile, for example, methyl hydroxybenzoate, anti-oxidants, flavorings, volatile oils, buffering agents and emulsifiers and other formulation surfactants.

The aerosols of solid particles comprising the active compound and surfactant may likewise be produced with any solid particulate medicament aerosol generator. Aerosol generators for administering solid particulate medicaments to a subject produce particles, which are respirable, as explained above, and generate a volume of aerosol containing a predetermined metered dose of a medicament at a rate suitable for human administration. One illustrative type of solid particulate aerosol generator is an insufflator. Suitable formulations for administration by insufflation include finely comminuted powders, which may be delivered by means of an insufflator or taken into the nasal cavity in the manner of a snuff. In the insufflator, the powder, e.g., a metered dose thereof effective to carry out the treatments described herein, is contained in capsules or cartridges, typically made of gelatin or plastic, which are either pierced or opened in situ and the powder delivered by air drawn through the device upon inhalation or by means of a manually-operated pump. The powder employed in the insufflator consists either solely of the active ingredient or of a powder blend comprising the active ingredient, a suitable powder diluent, such as lactose, and an optional surfactant. The active ingredient typically comprises from 0.1 to 100 % w/w of the formulation. A second type of illustrative aerosol generator comprises a metered

WHAT IS CLAIMED AS BEING NOVEL & UNOBVIOUS IN UNITED STATES LETTERS PATENT IS:

108. (Amended) An aerosolizable or sprayable [pharmaceutical] composition, comprising a carrier, a nucleic acid(s) [in the form of an aerosol] that comprise(s) one or more oligonuceleotide(s) (oligo(s)) effective to alleviate hyper-responsiveness to, and/or increased levels of, adenosine, and/or bronchoconstriction, and/or asthma, and/or lung allergy(ies) and/or lung inflammation, and/or to reduce levels of adenosine receptor(s) [and contains up to and including about 15% adenosine (A)], the oligo being anti-sense to an initiation codon, a coding region or a 5' or 3' intron-exon junction [s] of a gene(s) encoding an adenosine A_1, A_{2a}, A_{2b} or A_3 receptor(s) or being anti-sense to their corresponding [respective] mRNA(s), [;] pharmaceutically and veterinarily acceptable salts of the oligo(s) or mixtures thereof, and a surfactant that may be operatively linked to the nucleic acid; wherein when the adenosine receptor(s) comprise(s) an adenosine A_{2a} and/or A_{2b} receptor(s), the composition need not comprise a surfactant(s).

109. The composition of claim 108, wherein the oligo consists of up to about 10% A.

110. The composition of claim 109, wherein the oligo consists of up to about 5% A.

111. The composition of claim 110, wherein the oligo consists of up to about 3% A.

112. The composition of claim 111, wherein the oligo is A-free.

113. The composition of claim 108, wherein the oligo is anti-sense to the initiation codon of the mRNA, to the 5' or 3' intron-exon junctions or to sequences of the coding region comprising 2 or more G and/or C of the adenosine A_1 receptor gene.

114. The composition of claim 108, wherein the oligo is anti-sense to the initiation codon of the mRNA, to the 5' or 3' intron-exon junctions or to sequences of the coding region comprising 2 or more G and/or C of the adenosine A_{2a}, A_{2b} and/or A_3 receptors.

115. (Amended) The composition of claim 108, wherein if the oligo contains adenosine (A), at least one A is substituted by a universal base selected from [the group consisting of] heteroaromatic bases that bind to a thymidine base but have antagonist activity [and] or less than about 0.3 of the adenosine base agonist activity at the adenosine A_1, A_{2b} [and] or A_3 receptors, [and] or heteroaromatic bases that have no activity or have agonist activity at the adenosine A_{2a} receptor.

116. (Amended) The composition of claim 115, wherein substantially all As are substituted by a universal base (s) selected from heteroaromatic bases that bind to a thymidine base but either have antagonist activity or less than about 0.3 of the adenosine base agonist activity at the adenosine A_1, A_{2b} [and] or A_3 receptors, [and] or heteroaromatic bases that have no activity or have agonist activity at the adenosine A_{2a} receptor.

117. (Amended) The composition of claim 115, wherein the heteroaromatic bases are selected from pyrimidines or purines that may be substituted by O, halo, NH_2, SH, SO, SO_2, SO_3, COOH, or branched or fused primary or secondary amino, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkoxy, alkenoxy, acyl, cycloacyl, arylacyl, alkynoxy, cycloalkoxy, aroyl, arylthio, arylsulfoxyl, halocycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, alkynylcycloalkyl, haloaryl, alkylaryl, alkenylaryl, alkynylaryl, arylalkyl, arylalkenyl, arylalkynyl, or arylcycloalkl, which may be further substituted by O, halo, NH_2, primary, secondary or tertiary amine, SH, SO, SO_2, SO_3, cycloalkyl, heterocycloalkyl or heteroaryl.

118. The composition of claim 117, wherein the pyrimidines are substituted at a 1, 2, 3, and/or 4 position, and the purines are substituted at a 1, 2, 3, 4, 7 and/or 8 position.

119. (Amended) The composition of claim 118, wherein the pyrimidines or purines are selected from theophylline, caffeine, dyphylline, etophylline, acephylline piperazine, bamifylline, enprofylline or xanthine [xantine].

120. The composition of claim 116, wherein the universal base is selected from 3 – nitropyrrole-2'-deoxynucleoside, 5-nitroindole, 2-deoxyribosyl-(5-nitroindole), 2- deoxyribofuranosyl – (5 – nitroindole), 2' – deoxyinosine, 2' – deoxynebularine, 6H, 8H – 3, 4 – dihydropyrimido [4, 5 – c] oxazine – 7 – one or 2 – amino – 6 – methoxyaminopurine.

121. The composition of claim 108, wherein a methylated cytosine (^{m}C) is substituted for an unmethylated cytosine (C) in at least one CpG dinucleotide if present in the nucleic acid(s).

122. The composition of claim 108, wherein at least one monoculeotide is linked or modified by one or more of phosphorothioate, phosphorodithioate, phosphorotrithioate, methylphosphonate, phosphoramidate, boranophosphate, phosphotriester, formacetal, 2'-O- methyl, thioformacetal, 5'-thioether, carbonate, 5'-N-carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene (methylimino) (MMI) and methyleneoxy (methylimino) (MOMI), terminal 1,3-propanediol, terminal dodecanol, 2'-O- methoxyethyl, C-5-propynyl pyrimidine, C-5 methyl cytidine, C-5 ethynyl pyrimidine, 2' propoxy, C-18 amine, N3'-P5 phosphoramidates, 3'-alkylamino, 2'-fluoro; 5-fluoro pyrimidine, 5- iodo pyrimidine, 5-bromo pyrimidine, 2'-borano, C-5 hexynyl pyrimidine, 2'-O-(2-methoxy)ethyl, 2'-O-aminopropyl, 5-(phenylethyl) or peptide nucleic acid interbase linkages or conjugated to a polyethylene glycol, cholesterol, cholesteryl, dehydroepiandrosterone sulfatide (DHEA), dehydroepiandrosterone sulfate (DHEASulfate), dehydroepiandrosterone sulfatide (DHEASulfatide), ubiquinone (CoQn), dolichol, poly L-lysine, sulfatidic acid or fatty acids.

123. The composition of claim 122, wherein substantially all mononucleotides are linked or modified by one or more of phosphorothioate, phosphorodithioate, phosphorotrithioate,

methylphosphonate, phosphoramidate, boranophosphate, phosphotriester, formacetal, 2'-O- methyl, thioformacetal, 5'-thioether, carbonate, 5'-N-carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene (methylimino) (MMI) and methyleneoxy (methylimino) (MOMI), terminal 1,3-propanediol, terminal dodecanol, 2'-O- methoxyethyl, C-5-propynyl pyrimidine, C-5 methyl cytidine, C-5 ethynyl pyrimidine, 2'-propoxy, C-18 amine, N3'-P5' phosphoramidates, 3'-alkylamino, 2'-fluoro; 5-fluoro pyrimidine, 5-iodo pyrimidine, 5-bromo pyrimidine, 2'-borano, C-5 hexynyl pyrimidine, 2'-O-aminopropyl, 5-(phenylethyl) or peptide nucleic acid interbase linkages or conjugatd to a polyethylene, glycol, cholestrol, cholesteryl, dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEASulfate), dehydroepiandrosterone sulfatide (DHEASulfatide), ubiquinone (CoQn), dolichol, poly L-lysine, sulfatidic acid or fatty acids.

124. (Amended) The composition of claim 108, wherein the anti-sense oligo comprises [about] 7 to 60 mononucleotides.

125. (Amended) The composition of claim 108, wherein the oligo comprises a sequence selected from SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5 or DEQ ID NO: 7 to SEQ ID NO: [966] 998, or SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5 or SEQ ID NO: 7 to SEQ ID NO: [966] 998, wherein at least one mononucleotide is linked or modified by one or more of phoshporothioate, phosphorodithioate, phosphorotriester, formacetal, 2'-O-methyl, thioformacetal, 5'-thioether, carbonate, 5'-N-carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene (methylimino) (MMI) and methyleneoxy (methylimino) (MOMI), terminal 1,3-propanediol, terminal dodecanol, 2'-O-methoxyethyl, C-5-propynyl pyrimidine, C-5 methyl cytidine, C-5 ethynyl pyrimidine, 2'-propoxy, C-18 amine, N3'-P5' phosphoramidates, 3'-alkylamino, 2'-fluoro; 5-fluoro pyrimidine, 5-iodo pyrimidine, 5-bromo pyrimidine, 2'-borano, C-5 hexynyl pyrimidine, 2'-O-(2-methoxy)ethyl, 2'-O-aminopropyl, 5-(phenylethyl) or peptide nucleic acid interbase linkages or conjugated to a polyethylene glycol, cholesterol, cholesteryl, dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEA Sulfate), dehydroepiandrosterone sulfatide (DHEA Sulfatide), ubiquinone (CoQn), dolichol, poly L-lysine, sulfatidic acid or fatty acids.

126. The composition of claim 108, wherein the nucleic acid is linked to an agent that enhances cell internalization or up-take and/or a cell targeting agent.

127. The composition of claim 126, wherein the cell internalization or up take enhancing agent is a transferrin, asialoglycoprotein or a streptavidin.

128. The composition of claim 126, wherein the cell targeting agent comprises a vector, and the nucleic acid is operatively linked to the vector.

129. The composition of claim 128, wherein the vector comprises a prokaryotic or eukaryotic vector.

130. (Amended) The composition of claim 108, wherein the surfactant comprises surfactant proteins, phospholipids, fatty acids, or surfactant-associated proteins [is selected from surfactant protein A, surfactant protein B, surfactant protein C, surfactant protein D, surfactant protein D or active fragments thereof, non-dipalmitoyl disaturated phosphatidylcholine, dipalmitoylphosphatidylcholine, phosphatidylcholine, phosphatidylglycerol, phosphatidylinositol, phosphatidylethanolamine, phosphatidylserine, phosphatidic acid, ubiquinones, lysophosphatidylethanolamine, lysophosphatidylcholine, palmitoyl-lysophosphatidylcholin, dehydroepiandrosterone, dolichols, sulfatidic acid, glycerol-3-phosphate, dihydroxyacetone phosphate, glycerol, glycerol-3-phosphocholine, dihydroxyacetone, palmitate, cytidine diphosphate (CDP) diacylglycerol, CDP choline, choline, choline phosphate, lamellar bodies, omega-3 fatty acids, polyenic acid, polyenoic acid, lecithin, palmitic acid, non-ionic ethylene and/or propylene oxide block copolymers, polyoxypropylene, polyoxyethylene, poly (vinyl amine) with dextran and/or alkanoyl side chains, polyoxy ethylene ethers, phenoxy polyethoxy alcohols, phosphatidyl choline esters, phosphatidyl ethers, palmitates, tyloxapol, phospholipids, fatty acids, surfactant-associated proteins or $C_{22}H_{19}C_{10}$].

131. (Amended) The composition of claim 130, wherein the surfactant [is selected from] comprises polyoxy ethylene 23 lauryl ether (Brij 35®), t-octyl phenoxy polyethoxy ethanol (Triton X-100®), dipalmitoyl phosphatidyl choline (DPPC) and phosphatidyl glycerol (PG) (ALEC®), tyloxapol (Exosurf®), phospholipids, fatty acids, surfactant-associated proteins (Survanta®) or $C_{22}H_{19}C_{10}$ (Atovaquone®).

132. The composition of claim 108, wherein the carrier comprises a biologically acceptable carrier.

134. The composition of claim 108, wherein the carrier is a pharmaceutically or veterinarily acceptable carrier.

135. (Amended) The composition of claim 134, wherein the carrier is selected from [gaseous,] liquid or solid carriers.

136. The composition of claim 108, further comprising an agent selected from therapeutic agents other than the nucleic acid(s), antioxidants, flavoring or coloring agents, fillers, volatile oils, buffering agents, dispersants, RNA inactivating agents, flavoring agents, propellants or preservatives.

137. The composition of claim 136, comprising a pharmaceutically or veterinarily acceptable carrier, the nucleic acid, a surfactant, and other therapeutic agents.

138. The composition of claim 136, wherein the RNA inactivating agent comprises an enzyme.

139. The composition of claim 138, wherein the enzyme comprises a ribozyme.

140. The composition of claim 108, further comprising a propellant.

141. The composition of claim 108, wherein the nucleic acid is present in an amount of about 0.01 to about 99.99 w/w of the composition.

143. The formulation of claim 108, selected from intrabuccal, intrapulmonary, respirable, nasal, inhalable, intracavitary, intraorgan, or slow release formulations.

144. (Amended) The formulation of claim 143, wherein the carrier is selected from a [gaseous,] solid or liquid carrier.

146. (Amended) The [aerosol or spray] formulation of claim 108, which comprises a sprayable or aerosolizable [is selected from] powder [s, sprays], solution [s], suspension [s] or emulsion [s].

148. (Amended) The [aerosol or spray] formulation of claim 108, which comprises a sprayable or aerosolizable [is selected from] aqueous or alcoholic solution [s] or suspension [s], oily solution [s] or suspension [s], or oil-in-water or water-in-oil emulsion [s].

151. A capsule or cartridge, comprising the formulation of claim 143.

152. (Amended) The sprayable or aerosolizable formulation of claim 146, comprising a sprayable or aerosolizable solid powder [ed spray or aerosol].

153. The formulation of claim 108, wherein the carrier comprises a hydrophobic carrier.

158. (Amended) The formulation of claim 143, which comprises an intrapulmonary, intracavitary or intraorgan liquid or solid powdered formulation of particle size about 0.5μ to [about] 10 μ, or [about] 10 μ to [about] 500 μ.

159. (Amended) The formulation of claim 143, which comprises a nasal formulation of particle size [about] 10 μ to [about] 500 μ.

161. The formulation of claim 143, in bulk, or in single or multiple unit dose form.

162. (Amended) The formulation of claim 143, which is a respirable or inhalable formulation comprising a solid powdered or liquid aerosol or spray of particle size about 0.5 μ to [about] 10 μ.

163. A single cell, comprising the nucleic acid of claim 108.

164. (Amended) A diagnostic or therapeutic kit for delivery of an oligonucleotide(s) (oligo(s)) [diagnosis or treatment of diseases and conditions associated with hypersensitivity or and/or increased levels of, adenosine and/or adenosine receptor(s) and/or

bronchoconstriction and/or lung allergy(ies) and/or lung inflammation and/or asthma] comprising, in separate containers,

the delivery device of claim 222;

a nucleic acid comprising at least one oligonucleotide (oligo) [effective to alleviate hyper-responsiveness to, and/or increased levels of, adenosine, to alleviate bronchoconstriction, asthma lung allergy(ies) and/or lung inflammation, the oligo being anti-sense to the initiation codon, the coding region or the 5' or 3' intron-exon junctions of a gene encoding a protein associated with hyper-responsiveness to, and/or increased levels of, adenosine, with bronchoconstriction, asthma, lung allergy(ies) lung inflammation, or being anti-sense to the corresponding mRNA; the nucleic acid comprising one or more oligo(s)] , their mixtures or their pharmaceutically or veterinarily acceptable salts; and

instructions for preparation of a non-liposomal respirable, inhalable, nasal, intrapulmonary, intraorgan, or intracavitary formulations of the nucleic acid of particle size about 0.5 to [about] 500 μ and for its use; and

optionally an agent selected from therapeutic or diagnostic agents other than the oligo(s), anti-oxidants, fillers, volatile oils, dispersants, anti-oxidants, flavoring agents, propellants, preservatives, solvents, surfactants, buffering agents, RNA inactivating agents, agents that are internalized or up-taken by a cell, or coloring agents.

165. (Amended) The kit of claim 164, wherein the delivery device [comprises a nebulizer that] delivers single metered doses of a solid powdered or liquid aerosol or spray inhalable, respirable, intracavitary, intraorgan or intrapulmonary formulation of the nucleic acid of particle size about 0.5 μ to [about] 10 μ [or about 10 μ to about 500 μ of the nucleic acid].

166. (Amended) The kit of claim 164, wherein the device [comprises an insufflator] is adapted for receiving and piercing or opening a capsule(s) or cartridge(s) and producing a solid powdered or liquid aerosol or spray; and the nucleic acid is provided separately in a piercable or openable capsule(s) or cartridge(s) as a non-liposomal nasal, inhalable, respirable, intrapulmonary, intracavitary or intraorgan formulation of the nucleic acid [of particle size about 0.5 μ to about 10 μ or about 10 μ to about 500 μ].

167. (Amended) The kit of claim 164, wherein the delivery device comprises a pressurized [inhaler] device that delivers a solid powdered or liquid aerosol or spray of particle size about 0.5 μ to [about] 10 μ [or about 10 μ to about 500 μ]; and the nucleic acid is provided as a non-liposomal suspension, solution, emulsion or dry powdered aerosolizable or sprayable formulation of about 0.5 μ to [about] 10 μ [or about 10 μ to about 500 μ].

168. The kit of claim 164, comprising the delivery device, a surfactant, the nucleic acid and other therapeutic agents.

169. The kit of claim 164, wherein the solvent is selected from organic solvents or organic solvents mixed with one or more co-solvents.

170. (Amended) The kit of claim 164, wherein the device is adapted for receiving a capsule(s) or cartridge(s), and the nucleic acid is separately provided as a non-liposomal inhalable, respirable, nasal, intracavitary, intraorgan or intrapulmonary formulation in a capsule(s) or cartridge(s).

171. (Amended) The kit of claim 164 further comprising, in separate containers, a propellant, [and] pressurized means for delivery adapted for delivering a solid powdered or liquid aerosol or spray, and instructions for loading into the delivery device the nucleic acid as an inhalable, respirable, nasal, intracavitary, intraorgan or intrapulmonary formulation of particle size about 0.5μ to [about 10 μ or about 10 μ to about] 500 μ, and then joining the device with the propellant and the pressurized means.

172. The kit of claim 167, wherein the pressurized inhaler further comprises a propellant and means for delivery of the propellant, and delivers the nucleic acid as a liquid or solid powdered aerosol or spray formulation.

173. (Amended) An in vivo method of delivering a pharmaceutical composition to a target polynucleotide(s), comprising administering to the airways of a subject an aerosol or spray non-liposomal composition of particle size about 0.5 μ to [about 10 μ or about 10 μ to about] 500 μ comprising a nucleic acid(s) that comprises at least one oligonucleotide(s) (oligo(s))
[effective to alleviate hyper-responsiveness to, and/or increased levels of adenosine, or to alleviate bronchoconstriction, and/or asthma and /or lung allergy(ies) and/or lung inflammation, the oligo containing up to and including about 15% adenosine (A), and being anti-sense to the initiation codon, the coding region or the 5' or 3' intron-exon junctions of a gene encoding a protein associated with hyper-responsiveness to, and/or increased levels of, adenosine, bronchoconstriction, asthma and/or lung allergy(ies), and/or lung inflammation, or being anti-sense to the corresponding mRNA].

178. The method of claim 173, wherein the composition is administered intrapulmonary, intraorgan, intracavitarily, intrabuccally, intranasally, by inhalation or into the subject's respiratory system.

179. (Amended) The method of claim 173, wherein the oligo(s) is(are) anti-sense to the initiation codon, the coding region or the 5' or 3' intron-exon junctions of a gene encoding a protein associated with hyper-responsiveness to, and/or increased levels of, adenosine and/or levels of adenosine receptor(s), bronchoconsriction, asthma and/or lung allergy(ies), and/or lung inflammation, or being anti-sense to the corresponding mRNA, and is(are) effective to reduce hyper-responsiveness to adenosine,

and/or the amount of adenosine receptor(s) and/or the production or availability of adenosine, and/or to increase the degradation of the adenosine receptor(s) and/or its(their) mRNA(s).

180. The method of claim 178, wherein the oligo(s) is(are) administered directly into the subject;s lung(s), intraorgan, intracavitarily, intrabuccal or intrapulmonarily.

181. (Amended) The method of claim [178] 173, wherein the composition comprises solid powdered or liquid particles of the nucleic acid(s) about 0.5 to [about] 10 μ in size.

183. (Amended) The method of claim [181] 173, wherein the composition is administered as powdered solid or liquid nucleic acid particles [greater than about] 10 μ to 500 μ in size.

184. (Amended) The method of claim 173, further comprising administering [wherein the composition further comprises] a surfactant, which may be in the same composition as the nucleic acid.

185. (Amended) The method of claim [173] 179, wherein the hyper-responsiveness to and/or increased levels of, adenosine and/orlevels of adenosine (A) receptor(s), and/or asthma and/or lung allergy(ies) and/or lung inflammation is associated with bronchoconstriction, of lung airways.

186. (Amended) The method of claim 185, wherein the hyper-responsiveness to, or increased levels of, adenosine, levels of adenosine (A) receptor(s), and/or bronchoconstriction, and/or lung allergy(ies) and/or lung inflammation is(are) associated with COPD, asthma, ARDS, RDS,CF or side effects of adenosine administration.

187. (Amended) The method of claim [173] 179, wherein the hyper-responsiveness to, or increased levels of, adenosine, levels of adenosine (A) receptor(s), and/or bronchoconstriction, and/or asthma, and/or lung allergy(ies) and/or lung inflammation is(are) associated with inflammation or an inflammatory disease.

188. The method of claim 173, wherein the composition further comprises other therapeutic agents.

189. (Amended) The method of claim 188, wherein the therapeutic agent(s) comprise(s) anti-adenosine A_1, A_{2b} or A_3 receptor agents or adenosine A_{2a} receptor stimulating agents other than the nucleic acid(s).

190. (Amended) The method of claim [190] 184, wherein the surfactant comprises a surfactant protein, non-liposomal phospholipid, fatty acid, or surfactant-associated protein [surfactant protein A, surfactant protein B, surfactant protein C, surfactant protein D or active fragments thereof, non-dipalmitoyl disaturated phosphatidycholine, dipalmitoylphosphatidylcholine, phosphatidycholine, phosphatidylglycerol, phosphatidylinositol, phosphatidylethanolamine, phosphatidylserine, phosphatidic acid, ubiquinones, lysophosphatidylethanolamine,

lysophosphatidylcholine, palmitoyl-lysophosphatidylcholin, dehydroepiandrosterone, dolichols, sulfatidic acid, glycerol-3-phosphate, dihydroxyacetone phosphate, glycerol, glycerol-3-phosphocholine, dihydroxyacetone, palmitate, cytidine diphosphate (CDP) diacylglycerol, CDP choline, choline, choline phosphate, lamellar bodies, omega-3 fatty acids, polyenic acid, polyenoic acid, lecithin, palmitic acid, non-ionic ethylene and/or propylene oxide block copolymers, polyoxypropylene, polyoxyethylene, poly (vinyl amine) with dextran and/or alkanoyl side chains, polyoxy ethylene ethers, phenoxy polyethoxy alcohols, phosphatidyl choline esters, phosphatidyl ethers, palmitates, tyloxapol, phospholipids, fatty acids, surfactant-associated proteins or $C_{22}H_{19}C_{10}$].

192. The method of claim 173, wherein the subject is a mammal.

193. The method of claim 192, wherein the mammal is a human or a non-human mammal.

195. (Amended) The method of claim 173, wherein the nucleic acid is administered in an amount of about 0.005 to about 150 mg/kg body weight.

196. The method of claim 195, wherein the nucleic acid is administered in an amount of about 0.01 to about 75 mg/kg body weight.

197. The method of claim 196, wherein the nucleic acid is administered in an amount of about 1 to about 50 mg/kg body weight.

198. The method of claim 173, which is a prophylactic or therapeutic method.

200. (Amended) The method of claim [173] 179, wherein the nucleic acid is obtained by

(a) selecting fragments of a target nucleic acid having at least 4 contiguous bases consisting of G or C; and

(b) obtaining a second oligo 4 to 60 nucleotides long comprising a sequence that is anti-sense to the selected fragment

[, the second oligo having an A base content of up to and including about 15%] .

201. The method of claim 173, wherein the oligo consists of up to about 10% A.

202. The method of claim 201, wherein the oligo consists of up to about 5% A.

203. The method of claim 201, wherein the oligo consists of up to about 3% A.

204. The method of claim 203, wherein the oligo is A-free.

205. (Amended) The method of claim [173] 179, wherein the oligo is anti-sense to the initiation codon, the coding region or the 5' or 3' intron-exon junctions of a gene encoding an adenosine A_1, A_{2b} or A_3 receptor, and the composition may further comprise [s] a surfactant.

206. The method of claim 173, wherein if the oligo contains A, at least one A is substituted with a universal base selected from heteroaromatic bases which bind to a thymidine base but

have antagonist activity or less than about 0.3 of the adenosine base agonist activity at the adenosine A_1, A_{2b} or A_3 receptors, or heteroaromatic bases which have no activity or have agonist activity at the adenosine A_{2a} receptor.

207. (Amended) The method of claim 206, wherein substantially all As are substituted with universal bases selected from heteroaromatic bases which bind to a thymidine base but have antagonist activity or less than about 0.3 of the adenosine base agonist activity at the adenosine A_1, A_{2b} or A_3 receptors, or heteroaromatic bases which have no activity or have agonist activity at the adenosine A_{2a} receptor.

208. The method of claim 206, wherein the heteroaromatic bases are selected from pyrimidines or purines that may be substituted by O, halo, NH_2, SH, SO, SO_2, SO_3, COOH, branched fused primary secondary amino, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkoxy, alkenoxy, acyl, cycloacyl, arylacyl, alkynoxy, cycloalkoxy, aroyl, arylthio, arylsulfoxyl, halocycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, alkynylcycloalkyl, haloaryl, alkylaryl, alkenylaryl, alkynylaryl, arylalkyl, arylalkenyl, arylalkynyl, arylcycloalkl, all of which may be further substituted by O, halo, NH_2, primary, secondary and tertiary amine, SH, SO, SO_2, SO_3, cycloalkyl, heterocycloalkyl or heteroaryl.

209. The method of claim 208, wherein the pyrimidines are substituted at positions 1, 2, 3 and/or 4, and the purines are substituted at positions 1, 2, 3, 4, 7 and/or 8.

210. (Amended) The method of claim 209, wherein the pyrimidines and purines are selected from theophylline, caffeine, dyphylline, etophylline, acephylline piperazine, bamifylline, enprofylline or xanthine [xantine].

211. The method of claim 206, wherein the universal base comprises 3-nitropyrrole-2'-deoxynucleoside, 5-nitro-indole, 2-deoxyribosyl-(5-nitroindole), 2-deoxyribofuranosyl-(5-nitroindole), 2'-deoxyinosine, 2'-deoxynebularine, 6H, 8H-3,4-dihydropyrimido [4,5-c] oxazine-7-one or 2-amino-6-methodxyaminopurine.

212. The method of claim 173, further comprising methylating at least one cytosine vicinal to a guanosine into a methylated cytosine (^{m}C) if a CpG dinucleotide is present in the oligo(s).

213. The method of claim 173, further comprising modifying or substituting at least one mononucleotide of the anti-sense oligo(s) with methylphosphonate, phosphotriester, phosphorothioate, phosphorodithioate, boranophosphate, formacetal, thioformacetal, thioether, carbonate, carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene(methyimino), methyleneoxy (methylimino), 2'-O-methyl, phosphoramidate residues, or combinations thereof.

214. The method of claim 213, wherein substantially all mononucleotides are substituted and/or modified.

215. The method of claim 173, further comprising operatively linking the nucleic acid to an agent that enhances cell internalization or up-take, or a cell targeting agent.

216. The method of claim 215, wherein the cell internalization or up-take enhancing agent is selected from transferrin, asialoglycoprotein or streptavidin.

217. The method of claim 215, wherein the cell targeting agent comprises a vector.

218. The method of claim 217, wherein the vector to which the agent is operatively linked comprises a prokaryotic or eukaryotic vector.

219. (Amended) The method of claim [173] 179, wherein the nucleic acid comprises an oligo of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5 or SEQ ID NO: 7 to SEQ ID NO: 998 [966], or SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5 or SEQ ID NO: 7 to SEQ ID NO: 998 [966], wherein at least one mononucleotide is linked or modified by one or more of phosphorothioate, phosphorodithioate, methylphosphonate, phosphoramidate, boranophosphate, phosphotriester, formacetal, 2'-O- methyl, thioformacetal, 5'-thioether, carbonate, 5'-N-carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene (methylimino) (MMI) and methyleneoxy (methylimino) (MOMI), terminal 1,3-propanediol, terminal dodecanol, 2'-O-methoxyethyl, C-5-propynyl pyrimidine, C-5 methyl cytidine, C-5 ethynyl pyrimidine, 2' propoxy, C-18 amine, N3'-P5 phosphoramidates, 3'-alkylamino, 2'-fluoro; 5-fluoro pyrimidine, 5- iodo pyrimidine, 5-bromo pyrimidine, 2'-borano, C-5 hexynyl pyrimidine, 2'-O-(2-methoxy)ethyl, 2'-O-aminopropyl, 5-(phenylethyl) or peptide nucleic acid interbase linkages or conjugated to a polyethylene glycol, cholesterol, cholesteryl, dehydroepiandrosterone sulfatide (DHEA), dehydroepiandrosterone sulfate (DHEASulfate), dehydroepiandrosterone sulfatide (DHEASulfatide), ubiquinone (CoQn), dolichol, poly L-lysine, sulfatidic acid or fatty acids.

220. (Amended) The method of claim 191, wherein the surfactant [is selected from] comprises polyoxy ethylene 23 lauryl ether (Brij 35®), t-octyl phenoxy polyethoxy ethanol (Triton X-100®), dipalmitoyl phosphatidyl choline (DPPC) and phosphatidyl glycerol (PG) (ALEC®), tyloxapol (Exosurf®), phospholipids, fatty acids, surfactant-associated proteins (Survanta®) or $C_{22}H_{19}C_{10}$ (Atovaquone®).

221. (Amended) The method of claim [173] 179, wherein the hyper-responsiveness to, or increased levels of, adenosine, and/or increased levels of adenosine(A) receptor(s), and/or bronchoconstriction, and/or lung allergy(ies) and/or lung inflammation, is(are) associated with asthma or a disease or condition associated with asthma.

222. (Amended) A diagnostic or therapeutic device adapted for delivering a non-liposomal respirable, inhalable, nasal, intrapulmonary, intraorgan, or intracavitary formulation of particle size about 0.5 μ to about 500 μ, the formulation comprising a nucleic acid(s) that comprise(s) at least one oligonucleotide (oligo(s)), their mixtures, or their pharmaceutically or veterinarily acceptable salts. [effective for diagnosing or treating hyper-responsiveness to, or increased levels of, adenosine, bronchoconstriction, asthma, or lung allegy(ies) or lung inflammation, or a disease or condition associated with either of them, the oligo being anti-sense to the initiation codon, the coding region or the 5' or 3' intron-exon junctions of a gene encoding a protein associated with hyper-responsiveness to, or increased levels of, adenosine, bronchoconstriction, asthma, or lung allergy(ies) or lung inflammation, or being anti-sense to the corresponding mRNA(s); the nucleic acid(s) comprising one or more oligo(s), their mixtures, or their pharmaceutically or veterinarily acceptable salts.]

223. (Amended) The device of claim 222, [comprising a nebulizer] which is adapted for delivering single metered doses of the formulation as a solid powdered or liquid aerosol or spray of the nucleic acid of particle size about 0.5 μ to [about] 10 μ [or about 10 μ ti about 500 μ].

224. (Amended) The device of claim 222, which is [comprises an insufflator] adapted for receiving and piercing or opening a capsule(s) or cartridge(s), and for producing a solid powdered or liquid aerosol or spray of particle size about 0.5 μ to [about 10 μ or about 10 μ to about] 500 μ and wherein the formulation is provided separately in a piercable or openable capsule(s) or cartridge(s) as a nasal, inhalable, respirable, intrapulmonary, intracavitary or intraorgan formulation of particle size about 0.5 μ to [about 10 μ or about 10 μ to about] 500μ.

225. (Amended) The device of claim 222, which comprises a pressurized device [inhaler] that delivers a solid powdered or liquid aerosol or spray formulation of particle size about 0.5 μ to [about 10 μ or about 10 μ to about] 500 μ; wherein the formulation comprises a suspension, solution, emulsion or dry powder aerosol or spray of the nucleic acid.

226. (Amended) The pressurized device [inhaler] of claim 225 further [illegible] and propellant for delivery [illegible]

[illegible] propellants and propellant [illegible] wherein the [illegible] formulation as a liquid or solid powdered aerosol or spray.

228. The device of claim 222, which is adapted for receiving and piercing or opening a capsule(s) or cartridge(s), and wherein the formulation is provided separately in a capsule(s) or cartridge(s).

229. (Amended) The kit of claim 164, wherein the oligo(s) is(are) anti-sense to the initiation codon, the coding region or the 5' or 3' region of a gene encoding a polypeptide selected from an adenosine A_1 receptor, adenosine A_{2a} receptor, adenosine A_{2b} receptor, or adenosine A_3 receptor.

230. The kit of claim 229, for diagnosis or treatment of sepsis, pulmonary vasoconstriction, lung inflammation, or lung allergies, asthma, impeded respiration, respiratory distress syndrome (RDS), acute respiratory distress syndrome (ARDS), pain, cystic fibrosis (CF), pulmonary hypertension, pulmonary vasoconstriction, emphysema or chronic obstructive pulmonary disease (COPD).

231. (Amended) The kit of claim 164, wherein the nucleic acid comprises an oligo of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5 or SEQ ID NO: 7 to SEQ ID NO: 998 [966], or SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5 or SEQ ID NO: 7 to SEQ ID NO: 998 [966], wherein at least one mononucleotide is linked or modified by one or more of phosphorothioate, phosphorodithioate, methylphosphonate, phosphoramidate, boranophosphate, phosphotriester, formacetal, 2'-O- methyl, thioformacetal, 5'-thioether, carbonate, 5'-N-carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene (methylimino) (MMI) and methyleneoxy (methylimino) (MOMI), terminal 1,3-propanediol, terminal dodecanol, 2'-O- methoxyethyl, C-5-propynyl pyrimidine, C-5 methyl cytidine, C-5 ethynyl pyrimidine, 2' propoxy, C-18 amine, N3'-P5 phosphoramidates, 3'-alkylamino, 2'-fluoro; 5-fluoro pyrimidine, 5- iodo pyrimidine, 5-bromo pyrimidine, 2'- borano, C-5 hexynyl pyrimidine, 2'-O-(2-methoxy)ethyl, 2'-O-aminopropyl, 5-(phenylethyl) or peptide nucleic acid interbase linkages or conjugated to a polyethylene glycol, cholesterol, cholesteryl, dehydroepiandrosterone sulfatide (DHEA), dehydroepiandrosterone sulfate (DHEASulfate), dehydroepiandrosterone sulfatide (DHEASulfatide), ubiquinone (CoQn), dolichol, poly L-lysine, sulfatidic acid or fatty acids.

232. (Amended) The composition of claim 108, which comprises particle sizes of about 0.5 μ to [about 10 μ or about 10 μ to about] 500 μ.

233. The nucleic acid of claim 108, which is operatively linked to a vector.

234. (Amended) A single cell, comprising the nucleic acid(s) of claim 233.

Please add the following claims:

-- 235. The composition of claim 108, wherein the oligo(s) consist(s) of up to about 15% A.

236. The composition of claim 130, wherein the surfactant comprises surfactant protein A, surfactant protein B, surfactant protein C, surfactant protein D, surfactant protein E or active fragments thereof, non-dipalmitoyl disaturated phosphatidylcholine, dipalmitoylphosphatidylcholine, phosphatidylcholine, phosphatidylglycerol, phosphatidylinositol, phosphatidylethanolamine, phosphatidylserine, phosphatidic acid, ubiquinones, lysophosphatidylethanolamine, lysophosphatidylcholine, palmitoyl-lysophosphatidylcholin, dehydroepiandrosterone, dolichols, sulfatidic acid, glycerol-3-phosphate, dihydroxyacetone phosphate, glycerol, glycerol-3-phosphocholine, dihydroxyacetone, palmitate, cytidine diphosphate (CDP) diacylglycerol, CDP choline, choline, choline phosphate, lamellar bodies, omega-3 fatty acids, polyenic acid, polyenoic acid, lecithin, palmitic acid, non-ionic ethylene and/or propylene oxide block copolymers, polyoxypropylene, polyoxyethylene, poly (vinyl amine) with dextran and/or alkanoyl side chains, polyoxy ethylene ethers, phenoxy polyethoxy alcohols, phosphatidyl choline esters, phosphatidyl ethers, tyloxapol, or $C_{22}H_{19}C_{10}$.

237. The kit of claim 164, wherein the surfactant comprises surfactant protein A, surfactant protein B, surfactant protein C, surfactant protein D, surfactant protein E or active fragments thereof, non-dipalmitoyl disaturated phosphatidylcholine, dipalmitoylphosphatidylcholine, phosphatidylcholine, phosphatidylglycerol, phosphatidylinositol, phosphatidylethanolamine, phosphatidylserine, phosphatidic acid, ubiquinones, lysophosphatidylethanolamine, lysophosphatidylcholine, palmitoyl-lysophosphatidylcholin, dehydroepiandrosterone, dolichols, sulfatidic acid, glycerol-3-phosphate, dihydroxyacetone phosphate, glycerol, glycerol-3-phosphocholine, dihydroxyacetone, palmitate, cytidine diphosphate (CDP) diacylglycerol, CDP choline, choline, choline phosphate, lamellar bodies, omega-3 fatty acids, polyenic acid, polyenoic acid, lecithin, palmitic acid, non-ionic ethylene and/or propylene oxide block copolymers, polyoxypropylene, polyoxyethylene, poly (vinyl amine) with dextran and/or alkanoyl side chains, polyoxy ethylene ethers, phenoxy polyethoxy alcohols, phosphatidyl choline esters, phosphatidyl ethers, tyloxapol, or $C_{22}H_{19}C_{10}$.

238. The kit of claim 164, wherein the delivery device delivers single metered doses of a solid powdered or liquid aerosol or spray buccal, nasal, intracavitary, intraorgan or intrapulmonary formulation of the nucleic acid of particle size 10 μ to 500μ.

239. The kit of claim 164, wherein the delivery device is adapted for receiving and piercing or opening a capsule(s) or cartridge(s) and producing a solid powdered or liquid aerosol or spray;

and the nucleic acid is provided separately in a piercable or openable capsule(s) or cartridge(s) as an inhalable, respirable, intrapulmonary, intracavitary or intraorgan formulation of the nucleic acid(s) of particle size about 0.5 μ to 10 μ.

240. The kit of claim 164, wherein the delivery device is adapted for receiving and piercing or opening a capsule(s) or cartridge(s) and producing a solid powdered or liquid aerosol or spray, and the nucleic acid is provided separately in a piercable or openable capsule(s) or cartridge(s) as a buccal, nasal, intracavitary, intraorgan, or intrapulmonary formulation of particle size 10 μ to 500 μ of the nucleic acid.

241. The kit of claim 164, wherein the delivery device comprises a pressurized device that delivers a solid powdered or liquid aerosol or spray of particle size 10 μ to 500 μ; and the nucleic acid is provided as an aerosolizable or sprayable suspension, solution, emulsion or dry powder formulation of particle size 10 μ to 500 μ.

242. The kit of claim 164, wherein the nucleic acid is provided as a buccal, nasal, intracavitary, intraorgan, or intrapulmonary formulation of particle size 10μ to 500μ.

243. The kit of claim 171, wherein the nucleic acid is provided as an inhalable, respirable, intracavitary, intraorgan or intrapulmonary formulation of particle size about 0.5μ to 10μ.

244. The device of claim 222, being adapted for delivering a solid powdered or liquid aerosol or spray formulation of the nucleic acid of particle size 0.5μ to 10μ.

245. The device of claim 222, being adapted for delivering a solid powdered or liquid aerosol or spray formulation of the nucleic acid of particle size 10μ to 500μ.

246. The device of claim 222, being adapted for delivering single metered doses of the formulation as a solid powdered or liquid aerosol or spray of the nucleic acid of particle size 10μ to 500μ.

247. The device of claim 222, wherein the oligo(s) is(are) anti-sense to the initiation codon, the coding region or the 5' or 3' intron-exon junctions of a gene encoding a protein associated with hyper-responsiveness to, and/or increased levels of, adenosine and/or levels of adenosine receptor(s), bronchoconsriction, asthma and/or lung allergy(ies), and/or lung inflammation, or being anti-sense to the corresponding mRNA, and is(are) effective to reduce hyper-responsiveness to adenosine, and/or the amount of adenosine receptor(s) and/or the production or availability of adenosine, and/or to increase the degradation of the adenosine receptor(s) and/or its(their) mRNA(s).

248. The method of claim 190, wherein the surfactant comprises surfactant protein A, surfactant protein B, surfactant protein C, surfactant protein D, surfactant protein E or active fragments thereof, non-dipalmitoyl disaturated phosphatidylcholine, dipalmitoylphosphatidylcholine, phosphatidylcholine, phosphatidylglycerol, phosphatidylinositol, phosphatidylethanolamine, phosphatidylserine, phosphatidic acid, ubiquinones, lysophosphatidylethanolamine,

lysophosphatidylcholine, palmitoyl-lysophosphatidylcholin, dehydroepiandrosterone, dolichols, sulfatidic acid, glycerol-3-phosphate, dihydroxyacetone phosphate, glycerol, glycerol-3-phosphocholine, dihydroxyacetone, palmitate, cytidine diphosphate (CDP) diacylglycerol, CDP choline, choline, choline phosphate, lamellar bodies, omega-3 fatty acids, polyenic acid, polyenoic acid, lecithin, palmitic acid, non-ionic ethylene and/or propylene oxide block copolymers, polyoxypropylene, polyoxyethylene, poly (vinyl amine) with dextran and/or alkanoyl side chains, polyoxy ethylene ethers, phenoxy polyethoxy alcohols, phosphatidyl choline esters, phosphatidyl ethers, tyloxapol, surfactant-associated proteins or $C_{22}H_{19}C_{10}$.

249. The method of claim 173, wherein the oligo consists of up to about 15% A.

250. The method of claim 173, wherein the oligo(s) is(are) effective to alleviate hyper-responsiveness to, and/or reduce levels of adenosine or adenosine receptor(s), and/or to alleviate bronchoconstriction, and/or asthma and /or lung allergy(ies) and/or lung inflammation, the oligo containing up to and including about 15% adenosine (A), and being anti-sense to the initiation codon, the coding region or the 5' or 3' intron-exon junctions of a gene encoding a protein associated with hyper-responsiveness to, and/or increased levels of, adenosine and/or adenosine receptor(s), and/or bronchoconsriction, and/or asthma and/or lung allergy(ies), and/or lung inflammation, or being anti-sense to the corresponding mRNA.

251. The kit of claim 165, wherein the oligo(s) are effective to alleviate hyper-responsiveness to, and/or increased levels of, adenosine, and/or to alleviate bronchoconstriction, asthma and/or lung allergy(ies) and/or lung inflammation, and/or to reduce levels of adenosine receptor(s), the oligo being anti-sense to the initiation codon, the coding region or the 5' or 3' intron-exon junction of a gene(s) encoding a protein associated with hyper-responsiveness to, and/or increased levels of, adenosine, and/or levels of adenosine receptor(s), and/or with bronchoconstriction, and/or asthma, and/or lung allergy(ies) and/or lung inflammation, or being anti-sense to the corresponding mRNA(s); the nucleic acid comprising one or more oligo(s).

252. The kit of claim 164, wherein the oligo(s) are effective to alleviate hyper-responsiveness to, and/or increased levels of, adenosine and/or adenosine receptors, and/or to alleviate bronchoconstriction, asthma and/or lung allergy(ies) and/or lung inflammation, and/or to reduce levels of adenosine receptor(s), the oligo being anti-sense to the initiation codon, the coding region or the 5' or 3' intron-exon junction of a gene(s) encoding a protein associated with hyper-responsiveness to, and/or increased levels of, adenosine, and/or levels of adenosine receptor(s), and/or with bronchoconstriction, and/or asthma, and/or lung allergy(ies) and/or lung inflammation, or being anti-sense to the corresponding mRNA(s); the nucleic acid comprising one or more oligo(s); the kit being suitable for the diagnosis or treatment of a disease or condition associated with hypersensitivity to, and/or increased levels of,

adenosine and/or adenosine receptor(s), and/or bronchoconstriction and/or lung allergy(ies) and/or lung inflammation and/or asthma.

253. The method of claim 173, further comprising administering a surfactant.

254. The method of claim 253, wherein the surfactant is administered in a prophylactic or therapeutic amount. --.

s:\legal\00672\claims 02-6 (full set marked up)